



## A Single-Cell Transcriptomic Atlas of Human Neocortical Development during Mid-gestation.

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## **Public Summary:**

We performed RNA sequencing on 40,000 cells to create a high-resolution single-cell gene expression atlas of developing human cortex, providing the first single-cell characterization of previously uncharacterized cell types, including human subplate neurons, comparisons with bulk tissue, and systematic analyses of technical factors. These data permit deconvolution of regulatory networks connecting regulatory elements and transcriptional drivers to single-cell gene expression programs, significantly extending our understanding of human neurogenesis, cortical evolution, and the cellular basis of neuropsychiatric disease. We tie cell-cycle progression with early cell fate decisions during neurogenesis, demonstrating that differentiation occurs on a transcriptomic continuum; rather than only expressing a few transcription factors that drive cell fates, differentiating cells express broad, mixed cell-type transcriptomes before telophase. By mapping neuropsychiatric disease genes to cell types, we implicate dysregulation of specific cell types in ASD, ID, and epilepsy. We developed CoDEx, an online portal to facilitate data access and browsing.

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